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6. **AUTHORS OF REPORT: DRS. RP YEZIERSKI, C THOMAS, B CALANCIE, B NOGA**

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   Robert P. Yezierski, Ph.D. **Blair Calancie, Ph.D.**
   Christine Thomas, Ph.D. **Brian Noga, Ph.D.**

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13. ABSTRACT *(Maximum 200 words)*

The goal of Dr. Yezierski's research was to gain a better understanding of the anatomical, neurochemical and functional changes that occur within the central nervous system following spinal cord injury. During the funding period, efforts focused on changes within the injured spinal cord as well as on neurons at supraspinal sites. To survey the functional status of neurons at sites in cortical and subcortical structures three studies were initiated. These included efforts to evaluate changes in: (a) blood flow; (b) metabolic status; and (c) genetic expression in diencephalic structures following SCI. An investigation was completed of the physiological changes in spinal sensory neurons following injury. A study was also completed in which a comparison was made between the excitotoxic properties of NMDA and AMPA in an effort to further characterize the pathological consequence of different EAA receptor agonists in SCI.

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SENSORY AND MOTOR RESPONSES TO SPINAL CORD INJURY

Dr. Robert P. Yezierski (PRINCIPAL INVESTIGATOR): SENSORY CONSEQUENCES OF SPINAL CORD INJURY

The goal of Dr. Yezierski's research was to gain a better understanding of the anatomical, neurochemical and functional changes that occur within the central nervous system following spinal cord injury. During the funding period efforts focused on changes within the injured spinal cord as well as on neurons at supraspinal sites. To survey the functional status of neurons at sites in cortical and subcortical structures three studies were initiated. These included efforts to evaluate changes in: (a) blood flow; (b) metabolic status; and (c) genetic expression in diencephalic structures following SCI. Additionally, in order to establish behavioral correlates of these changes we investigated the onset and progression of pain related behavioral changes which are believed to be an important manifestation of changes in the functional state of spinal and supraspinal neurons following spinal cord injury. The behavioral testing protocols used in these studies involve the testing of spinal injured animals with calibrated thermal and mechanical stimuli. In addition to evaluating the effects of injury on behavioral changes we measured the ability of different interventions to prevent the onset or reduce the progression of different pain related behaviors. Collectively, this work represents efforts to develop and characterize sensory disturbances produced by an excitotoxic model of spinal cord injury (SCI) and to begin the development of therapeutic strategies for the treatment of these conditions.

In the blood flow and metabolic studies mentioned above animals undergoing excitotoxic injury and which developed spontaneous and evoked pain related behaviors were being evaluated. The rationale for these studies focuses on the contention that if pain related behaviors reflect the onset of abnormal sensory states, e.g. central pain, they should produce changes in blood flow and metabolic state in brain regions involved in the processing of somatosensory information. Changes in blood flow are, therefore, believed to reflect changes in the neuronal excitability and spontaneous activity of neurons in these regions of the brain. Another study that was carried out focused on the evaluation of changes in mRNA expression in supraspinal structures. The results of these studies are being used in the design of electrophysiological studies to be carried out with the intention of identifying neurophysiological correlates of spontaneous and evoked pain related behaviors.

In addition to the above studies we completed an investigation of the physiological changes in spinal sensory neurons following injury. In this study significant changes in the response properties of spinal neurons adjacent to a site of injury, including an increase in excitability and background activity, and the development of long after discharge responses following removal of a stimulus were observed. A manuscript describing this work is in preparation. A study was also completed in which a comparison was made between the excitotoxic properties of NMDA and AMPA in an effort to further characterize the pathological consequence of different EAA receptor agonists in SCI.

A complete list of the publications submitted or published during the funding period is included below.

PAPERS IN REFEREED JOURNALS:

1. Reina, L.A. and Yezierski, R.P. A combined behavioral and physiological method for the assessment of thermosensation in the rat. J. Neurosci. Methods, 63:185-195, 1995.

2. Yezierski, R.P., Liu, S., Ruenes, G.L., Busto, R., and Dietrich, D. Neuronal damage following intraspinal injection of a nitric oxide synthase inhibitor in the rat. J. Cereb. Blood Flow and Metab., 16:996-1004, 1996.

3. Yezierski, R.P. Pain following spinal cord injury: the clinical problem and experimental studies. Pain 68:185-194, 1996.

4. Liu, S., Ruenes, G.L. and Yezierski, R.P. NMDA and non-NMDA receptor antagonists protect against excitotoxic injury in the rat spinal cord. Brain Res. 756 (1997) 160-167.

5. Brewer, K.L., and Yezierski, R.P. Effects of adrenal medullary chromaffin cell transplants on pain related behaviors following excitotoxic spinal cord injury. Brain Research 798 (1998) 83-92.

6. Dora, C., Koch, S., Ruenes, G.L., Sanchez, A., and Yezierski, R.P. Effects of adenosine on neuronal damage produced by intraspinal or intrathecal injection of the nitric oxide synthase inhibitor L-NAME. J. Neurotrauma 15 (1998) 473-483.

7. Yezierski, R.P., Liu, S., Ruenes, G.L., Kajander, K.J., Brewer, K.L. Excitotoxic spinal cord injury: behavioral and morphological characteristics of a central pain model. Pain 75 (1998) 141-155.

8. Schwartz, ED, Yezierski, RP, Quencer, RM, Pattany, PM, Weaver, RG MR and diffusion weighted imaging of syringomyelia following excitotoxic spinal cord injury. American J. Radiology (IN PRESS).

9. Brewer, K.L., Bethea, J.L. and Yezierski, R.P. The neuroprotective effects of IL-10 following excitotoxic spinal cord injury. Expt. Neurology (IN PRESS).

10. Morrow, TJ, Paulson, PE, Brewer, KL, Yezierski, RP, Casey, KL Chronic, selective forebrain responses to excitotoxic dorsal horn injury. Expt. Neurol. (Submitted).

11. Yezierski, RP and Brewer, KL Functional state of spinal sensory neurons following excitotoxic spinal cord injury in the rat (in preparation).

Dr. Brian Noga (INVESTIGATOR): MOTOR CONSEQUENCES OF SPINAL CORD INJURY

Dr. Brian Noga from the Department of Physiology at the University of Manitoba was hired as an Assistant Professor in the Department of Neurological Surgery and The Miami Project with the DOD research funds. Dr. Noga arrived in April of 1996 to begin the planning of a new laboratory for the study of brain and spinal cord mechanisms involved in the initiation and control of locomotor movements. The actual construction/renovation of the new laboratory began in mid September and was completed at the end of that year. Procurement and setup of equipment for the laboratory continued until March 1998. A fair proportion of the electronic equipment was custom built along the lines of successful models used in other laboratories performing this type of work. A description of the laboratory and its equipment is given below. A number of projects were initiated and two are near completion. Publications from these projects are listed below. A description of other ongoing research in the lab is also given.

Project 1: Restoration of function following spinal cord injury is possible providing there is a functional reconnection of the isolated spinal cord to higher control centers of the brain by axons regenerating through or past the site of injury. The purpose of this research was to assess the functionality of regenerated axons by measuring electrophysiologically their ability to conduct signals or action potentials through implanted guidance channels bridging a spinal cord transection. This research was conducted in collaboration with Drs. Blair Calancie and Alberto Pinzon, a Graduate Student from the Department of Biomedical Engineering. Dr. Pinzon's Thesis is entitled **"Electrophysiological Assessment of Neural Regeneration in Guidance Channels"**. The experimental work was largely conducted in the laboratory of Dr. Noga. The study was completed in rats and demonstrated that compound action potentials could be measured from functional axons regenerated through guidance channel implants. The ability to measure these signals was related to the number of regenerated axons. It is concluded that the electrophysiological technique employed in this study can be used for a functional assessment of axon regeneration in guidance channel implants and possibly other regeneration protocols in which there is a large number of regenerating axons.

Project 2: The inability to initiate and/or control walking is a defining sequella of most serious spinal cord injuries. In mammals, the spinal cord contains a neuronal network that can produce the basic patterns of stepping in the absence of input from the brain. Fortunately, these networks can be activated pharmacologically by a class of neuroactive substances known as monoamines, which are normally released in the spinal cord by terminals of neurons whose cell bodies are located in the brainstem. This fact indicates the potential usefulness of *monoaminergic transmitter replacement therapy* for the improvement of locomotor function following SCI. Our understanding of how descending monoaminergic neurons normally act on spinal locomotor networks, however, is limited by the lack of information regarding where monoamines are normally released in the spinal cord and on which neurons and membrane receptors these substances exert their various actions. As a first step in determining this information, experiments were conducted to investigate the sites of release of monoamines during locomotion. This research was conducted solely in the PI's laboratory in collaboration with Mr. Riza Mesigil, a Graduate Student from the Department of Biomedical Engineering. Mr. Mezigil's Master's Thesis is entitled **"The Design and Application of Carbon Fiber-based Microdimensional Biosensors for in Vivo Detection of Neurotransmitters (Monoamines) in the Cat Spinal Cord"**. Using a relatively new technique for the real-time measurement of monoamine transmitter release (fast cyclic voltammetry), we successfully developed a sensitive carbon-fiber microelectrode biosensor and measured the release of monoamines in the spinal cord during locomotion evoked by electrical stimulation of the brainstem. To date we have detected serotonin and noradrenaline release at localized sites within the lumbar spinal cord controlling hindlimb locomotor activity in the cat. The release has been detected in areas known to contain locomotor-activated neurons and in other areas where its release may be important for the inhibition of unwanted reflex circuits which could interfere with the smooth progression of movement. This release is detectable within 8 seconds of the onset of locomotion and is the first demonstration of the temporal correlation between monoamine release and locomotion. Once related to changes in monoamine receptor distribution that occur following SCI, this information will provide us with a better understanding of where drug therapies for the improvement of locomotor function following SCI could be effectively applied. It will also aid in the design of delivery systems/methods for the administration of these neurochemicals to specific regions of the spinal cord in individuals with SCI.

Project 3. Walking in mammals is achieved through the activation of spinal neurons by the reticulospinal pathway originating in the brainstem. Our understanding of how the spinal centers for the production of walking are activated and generate locomotor movement is limited, however, by our lack of information concerning the anatomical relationship between the descending pathway and its target neurons within the spinal cord and the pharmacology of this interaction. This information is essential for our understanding of how to drive the intrinsic rhythm generators of the distal cord since it will reveal the sites of termination of the locomotor pathway, the location of the neurons activated by this pathway, and the neurotransmitters involved in the production of locomotor activity. An investigation of the anatomy of the descending pathway terminations and the location of the target neurons receiving contacts from this pathway is presently underway. We have injected the anterograde neuroanatomical tracer, biotinylated dextran amine, into the site of origin of the descending locomotor reticulospinal pathway. The animals have been subsequently subjected to an extensive locomotor paradigm to express the nuclear protein c-fos to label locomotor-activated spinal neurons. The spinal cords from these animals are presently being processed immunohistochemically to determine the location of the locomotor-activated target neurons receiving contacts from the descending locomotor pathway. In another series of experiments, we have retrogradely labeled reticulospinal neurons following spinal injections of various fluorescent tracers in animals subject to activity dependent labeling using c-fos immunohistochemistry. We are presently analyzing this tissue to determine the phenotype of the descending locomotor pathway. This information will also provide us with a better understanding of where drug therapies for the improvement of locomotor function following SCI could be effectively applied.

RESOURCES (Brain Noga, Ph.D.):

Office: The PI maintains a 100 sq ft office within the laboratory. The office contains adequate desk space, a PC workstation and adequate shelving. The PI is the only occupant.

Laboratory: The PI's laboratory for conducting all acute electrophysiological experiments in the area of spinal cord research occupies about 850 sq. ft within the Miami Project. The laboratory is fully equipped from funding provided by the DOD. It has a surgery and an electrophysiology area. The laboratory is located in the same building as the Department of Veterinary Resources of the University of Miami where the specialized surgical procedures requiring sterile surgery and survival periods are performed on the animals. The laboratory is located next door to the Miami Project's Image Analysis Suite where the anatomical analysis for these and other experiments will be performed. The laboratory space is for the exclusive use of the PI and there is adequate work space for up to 4 investigators; currently, there is desk and work space for the PI, a postdoctoral associate, a technician and one Masters student.

Property Report (Brian Noga, Ph.D.):

Computer Equipment: The PI has a terminal PC workstation (Pentium) in his office facility. In addition, the PI has five 233 MHz Pentium computers (4 GB) in the laboratory, three of which are used in data capture/analysis, the remainder used exclusively for data analysis/graphics and word processing. The primary software used for data capture and analysis of electrophysiological data was purchased from the Spinal Cord Research Centre, at the University of Manitoba (Winnipeg, Canada). This program is capable of capturing up to 16 channels of data in excess of 20 kHz and storing all data to disk. The analysis program can perform over 50 basic types of analysis and/or processing of the captured data. It meets or exceeds the requirements of the

types of experiments done in the laboratory. The PI also has a "camera" software program developed at the Spinal Cord Research Centre (University of Manitoba), capable of capturing and analyzing up to four triggered signals. The PI has a commerically available software (Axoscope, Axon Instruments) for monitoring electroneurogram activity during evoked locomotion. Other computer-related equipment purchased with DOD funds include: a 2GB, 166 MHz notebook computer, a HP ScanJet 4C, a CD-rom writer, an internal and external Jaz Drive, a HP 1000 CSE color printer and a Fargo Dye Sublimation printer. All computers and printers, etc. are linked by network, providing the capability of data analysis (etc.) at any computer workstation.

EQUIPMENT (Brian Noga, Ph.D.):

Surgical/Animal Monitoring Equipment: All necessary anaesthesia/surgical equipment for the proposed experiments is available within the PI's laboratory (with Matrix halothane vaporizer and an Engler Anesthetic Delivery System). The PI also has two feedback-controlled heating lamps, two blood pressure monitors and a Datex Oscaroxy airway gas monitor (for N_2O, CO_2, O_2 and PaO_2 tissue oxygenation measurements). A Baker FH48G fume/exhaust hood is adjacent to the surgical preparation area.

Electrophysiology/Lab Equipment: Located in the PI laboratory, the electrophysiology setup consists of a number of components: **a)** a complete Transvertex cat electrophysiology frame including: two micromanipulator frames (spinal arcs); three microdrives (micromanipulators) and control units; a piggyback microelectrode holder adaptor; two stereotaxic instruments; and three stimulating/recording electrode holders; **b)** an Axoclamp 2B dual microelectrode amplifier with Axoclamp Interface (with dual pulse generator for extended current pulse control); **c)** a Millar Voltammeter (PD Systems) capable of high resolution and high speed fast cyclic voltammetry for the real-time measurement of transmitter release from sites within the spinal cord; **d)** two 4 channel digital Tectronix (420A) oscilloscopes; **e)** an oscilloscope interface; **f)** a Vetter PCM Recording Adaptor (for A/D and D/A conversion of data to tape for off-line analysis) and Sony SLV-685HF VCR; **g)** a three channel switchable constant current or voltage Eide stimulator with starter/delay/train unit; **h)** an alternator (for controlling or alternating the stimulator sequences); **i)** 12 channel low noise differential amplifier; **j)** a window discriminator; **k)** a 16 channel sound mixer; **l)** computerized camera controller; **m)** Stanford Research Systems (DS335) Function Generator; **n)** Mettler/Toledo Analytical Balance; **o)** Polyscience Refrigerated Circulating Water Bath; and **p)** a Zeiss AxioLab microscope.

Dr. Christine K. Thomas (INVESTIGATOR): MUSCLE SPASTICITY AFTER HUMAN SPINAL CORD INJURY

Specific Aims: In individuals with chronic spinal cord injury (SCI), we proposed to:
1. Characterize the patterns of muscle activity during spasms.
2. Examine the modulation of reflexes in response to the acute induction of spasticity.
3. Determine whether spasms can be influenced by supraspinal input.

Progress: Five issues have been addressed:
1. A manuscript has been published that describes distinct patterns of motor unit activity unit behavior during muscle spasms in spinal cord injured subjects. In brief, surface EMG and force were recorded during repeated involuntary spasms of paralyzed triceps surae muscles of four men with chronic cervical spinal cord injury.

The firing rates of 78 medial gastrocnemius (MG) motor units were also recorded intramuscularly with tungsten microelectrodes. Spasms typically involved a relatively rapid rise, then a more gradual fall in triceps surae EMG and torque. Motor unit firing rates either increased and then decreased with the spasm intensity (54 %), or were relatively constant (26 %), firing mainly at 2-10 Hz. The remaining units (20 %) produced trains which included one or several doublets. Mean (± SD) peak spasm firing rates were 18 ± 9 Hz for rate modulated units and 11 ± 10 Hz for units with little or no rate modulation. Some motor units fired at rates comparable to those recorded previously during maximum voluntary contractions performed by intact subjects. Others fired at rates below the minimum usually seen when normal units are first recruited (<6 Hz). Doublets (inter-spike interval <10 ms) often repeated every 123-333 ms, or were interspersed in trains firing at low steady rates (<11 Hz). This study shows that rate coding for many motor units appears to be similar whether descending motor input is intact or whether it has been reduced severely by spinal cord injury. In contrast, rate modulation in other units appears to depend mainly on voluntary motor commands.

2. A second paper has been published in which the electrical and mechanical properties of paralyzed human thenar muscles were measured in response to supramaximal stimulation of the median nerve in individuals with chronic cervical spinal cord injury. These data were compared to those recorded from control muscles. In all but two of the experiments performed on SCI subjects (94 %, 15 subjects), spontaneous motor unit activity which the subject was unable to stop and which did not depend on whether or not the muscle was being stimulated was seen in otherwise paralyzed thenar muscles. In general, the mean firing rate of spontaneously active motor units was low, but there were occasional, short interspike intervals corresponding to rates up to 20 Hz. Thus, chronic paralysis consequent to SCI did not render most human thenar muscles inactive. Those units which fired spontaneously at low but steady rates (4-8 Hz) exerted either no discernable force or weak forces (12-52 mN). Stronger forces were generated by those units which fired only occasionally, at rates of less than 1 Hz (161-233 mN). The force from these strong units produced visible muscle shortening. Interestingly, almost half the paralyzed muscles showed no sign of weakness judged by their tetanic forces. Between the extremes of normal muscle strength and complete dysfunction were ten other paralyzed muscles which were significantly weaker than the average control muscle. Those subjects with paralyzed muscles of normal strength reported that their muscles often underwent frequent involuntary muscle spasms. These data suggest that the neural activity caused by spasticity, frequent involuntary muscle spasms, reflexes and continuous motor unit activity in the "relaxed" state may be sufficient to counter disuse in some paralyzed muscles but not in others.

3. A manuscript has been submitted which describes motor unit recruitment and rate modulation during clonus. These data were also presented at a symposium entitled, "Peripheral and Spinal Mechanisms in the Neural Control of Movement". In summary, medial gastrocnemius surface and intramuscular EMG were recorded during clonus in six individuals with chronic cervical spinal cord injury to document the recruitment order and rate modulation of motor units during these repeated involuntary contractions. All subjects were free of spasm reducing medication, had no voluntary control of leg muscles, and were able to induce clonus in leg muscles that ranged in frequency from 4.7-7.0 Hz. Four subjects evoked spasms that stopped spontaneously within 1-30 s. In two subjects clonus was actively stopped after one minute by passive limb movement or the application of external force. Most of the 424 motor units (402 or 95 %) recorded during clonus fired once during each clonus cycle so the mean firing frequency was close to the clonus frequency and rate modulation was negligible. Four motor units (<1 %) fired during some clonus cycles, while 18 motor units (4 %) fired irregularly at higher frequencies (21-124 Hz). Only four of these units generated doublets

(interspike interval ≤ 10 ms). When 99 pairs of units were monitored over repeated clonus cycles (n=5-219), only 15 pairs of units altered their recruitment order. These data show that there are powerful spinal mechanisms that underlie the orderly recruitment of motor units during involuntary contractions of human muscles that lack descending inputs from higher centers.

4. Patterns of leg muscle activity during clonus have been documented and presented as a poster at the Neural Control of Movement meeting. In brief, extensors and flexors usually contracted in phase, but alternating bursts of antagonistic muscle activity were sometimes present. Two subjects had clonus for minutes, with EMG magnitude, cycle duration and burst duration relatively constant throughout. Clonus in another subject lasted 30 s and weakened and slowed progressively. The other subjects had tonic spasms interrupted by 5-22 cycles of clonus. Cycle duration varied in different subjects from 145-205 ms. Burst duration lasted 45-60 ms. Soleus H-reflexes were also monitored during clonus to assess whether these repeated involuntary contractions involved modulation of the exaggerated H-reflex already present in people with chronic cervical spinal cord injury. Tibial nerve stimulation did not change clonus intensity or frequency but did reset the onset of the cycle — an EMG burst followed by relative EMG silence (inter-burst). Clonus lasted from 1 s to > 60 s in six subjects but there was no correlation between the number of clonic beats and the maximal H-reflex to M-wave ratios at rest. H-reflex amplitude was minimal after each EMG burst, the time peak clonus force was attained. It rose at burst onset, sometimes exceeding the maximal M-wave at rest. Only 2 ± 1 % of the H-reflex modulation during clonus related to the 15 ± 3 degree changes in ankle angle. With pairs of stimuli each H-reflex was of similar magnitude at frequencies <5 Hz. The second H-reflex was often potentiated at clonus frequencies (5-8 Hz) but declined at frequencies >10 Hz. H-reflex modulation with paired stimulus pulses was similar to that during clonus, further support that clonus after chronic cervical spinal cord injury involves repeated stretch reflexes. A manuscript that describes these data is in preparation.

5. We have performed another series of experiments in which involuntary muscle contractions or spasms of three types have been characterized in upper limb muscles of individuals with chronic cervical spinal cord injury (SCI). These data were presented at the Society for Neuroscience meeting and are currently being prepared for publication. The spasms involved: a) brief bursts of involuntary muscle activity lasting up to 5 s; b) spontaneous motor unit activity at low firing rates (<10 Hz) ; and c) myoclonic-like spasms that repeat at 0.5 Hz, approximately five times slower than classical clonus. The bursts of involuntary EMG activity lasted up to 1 s and repeated every 2 s for up to 6 minutes. Cycle duration was similar across subjects, was reproducible from day to day, and was not interrupted by peripheral nerve stimulation or voluntary contractions. During these involuntary contractions, some triceps brachii motor units showed rate modulation in accord with the general rise and fall in muscle excitability. Other motor units showed little or no rate modulation. Minimum and maximum motor unit firing rates ranged from 1-15 Hz and 2-20 Hz respectively. Rate modulation varied up to 3-fold for different motor units. When two of these subjects performed voluntary triceps brachii contractions, minimum and maximum motor unit firing rates were higher, ranging from 9-21 Hz and 13-67 Hz respectively. Rate modulation for different motor units varied between 1.2 to 5.6-fold. These data show that different stimuli can excite the injured spinal cord to produce stereotyped involuntary muscle output which cannot be interrupted easily. The motor unit rate modulation that underlies these involuntary contractions can be as substantial as that measured during voluntary muscle contractions, but it occurs at lower absolute rates.

PAPERS IN REFEREED JOURNALS:

Thomas CK, and Ross BH. Distinct patterns of motor unit behavior during muscle spasms in spinal cord injured subjects. J. Neurophysiol. 1997, 77:2847-2850.

Thomas CK. Contractile properties of human thenar muscles after chronic cervical spinal cord injury. Muscle and Nerve, 1997, 20:788-799.

Wallace D, Ross BH, Kozhina GV, and **Thomas CK.** Motor unit recruitment and rate modulation during clonus. J. Neurophysiol. 1999, submitted.

OTHER PUBLICATIONS:

Wallace D, Kozhina GV, Ross BH, and **Thomas CK.** Motor unit behavior during clonus after human SCI. Peripheral and Spinal Mechanisms in the Neural Control of Movement Symposium, 1998.

Kozhina GV, Ross BH, Wallace D, and **Thomas CK.** Clonus in leg muscles after human spinal cord injury, Neural Control of Movement meeting, 1998.

Thomas CK, Esipenko VB, and Ayyar DR. Motor unit activity during myoclonus in spinal cord injured subjects. Neurosci. Abs. 1997, 23:1832.

Ross BH, Kozhina GV, Wallace D, and **Thomas CK.** H-reflex modulation during clonus. 1999, in preparation.

Thomas CK, Esipenko VB, and Ayyar DR. Motor unit rate modulation during slow, repeated spasms in spinal cord injured subjects. 1999, in preparation.

Dr. Blair Calancie (INVESTIGATOR): MOTOR CONSEQUENCES OF SPINAL CORD INJURY

Dr. Calancie's report submitted to the PI for inclusion in the final report consisted of the following statement. If additional information is desired I would suggest that you contact him directly at The Miami Project, University of Miami, Miami, Florida.

"There were no papers generated and no abstracts submitted for publication. There were no adverse events with respect to human experimentation. A research grant developed from preliminary data generated through the DOD funding has been awarded by "National Institute of Child Health and Human Development; National Center for Medical Rehabilitation Research" for the project entitled "Body Weight Supported Ambulation Training after Spinal Cord Injury". This is a 5-year award, with total direct costs of $1,600,885. It is a randomized, 3-arm trial which utilizes body weight support in 2 of the 3 training arms, and targets persons with chronic, neurologically-incomplete spinal cord injury."